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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/244,984	02/04/1999	ROY A. BLACK	16761/153	4402

7590 01/11/2002
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EXAMINER

ZEMAN, MARY K

ART UNIT	PAPER NUMBER
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1631

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DATE MAILED: 01/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/244,984

Applicant(s)

BLACK ET AL.

Examiner

Mary Zeman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41-43 and 45-66 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41-43 and 45-66 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Continued Prosecution Application

The request filed on 10/22/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/244984 is acceptable and a CPA has been established. An action on the CPA follows.

Claims 41-43 and 45-66 are pending in this application. Claim 66 is newly added.

The replacement sections for the specification have been entered. The paper requesting the transfer of the CRF from a related application is being processed.

The IDS filed 10/22/01 has been entered and considered. An initialed copy of the PTO 1449 is included with this action.

The declaration of Dr. Barone under 37 CFR 1.132 filed 10/12/01 is insufficient to overcome the rejection of claims 41-65 based upon 35 USC 112, first paragraph, scope of enablement as set forth in the last Office action and will be addressed below.

Drawings

Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect may be deferred until after the examiner has considered the proposed drawing correction. The PTO-948 Draftsman's Drawing Review was mailed with paper No. 9, mailed 8/3/00. If applicant requires a copy of this form, one can be provided. Failure to timely submit the proposed drawing correction will result in the abandonment of the application.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 41-43 and 45-65 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

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The claims are drawn to methods which only manipulate data, with no concrete application outside of the computer on which the method can be performed.

MPEP 2106 addresses computer-implemented inventions: "To be statutory, a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical application in the technological arts is either disclosed in the specification or would have been known to a skilled artisan (discussed in i) below), or (B) be limited by the language in the claim to a practical application within the technological arts." "The claimed practical application must be a further limitation upon the claimed subject matter if the process is confined to the internal operations of the computer. If a physical transformation occurs outside the computer, it is not necessary to claim the practical application. A disclosure that permits a skilled artisan to practice the claimed invention, i.e., to put it to a practical use, is sufficient. On the other hand, it is necessary to claim the practical application if there is no physical transformation or if the process merely manipulates concepts or converts one set of numbers into another."

Claims 41-43 and 45-65 do not recite statutory computer-implemented processes. Claim 63 recites a method of acting of a set of data (atomic coordinates) and using them to virtually design and virtually test for binding ability. As set forth in MPEP 2106: If the "acts" of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the facts are not being applied to appropriate subject matter. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process. This has also been addressed by the courts: a process that simply manipulates abstract ideas without some claimed practical application is non-statutory, e.g., a bid (Schrader, 22 F.3d at 293-94, 30 USPQ2d at 1458-59) or a bubble hierarchy (Warmerdam, 33 F.3d at 1360, 31 USPQ2d at 1759).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 41, 42, 45-63 and 66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of designing TACE-associating compounds using the particular atomic coordinates listed in Table 1, does not reasonably provide enablement for the breadth of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has submitted the declaration of Dr. Barone to address this rejection. This declaration is insufficient to obviate this rejection. The declaration states that the specific disclosed coordinates of Table 1 of the instant invention were used to design a number of TACE-associating compounds, which were then tested for association and inhibition in a variety of in vitro assays. This showing is not commensurate in scope with the rejected claims. The rejected claims do not require the particular atomic coordinates recited in Table 1.

As set forth previously, the specification discloses the co-crystallization of a particular associating compound with a specific, non-native TACE. A particular set of atomic coordinates is generated from this particular co-crystal. (Table 1) The truncated and mutated TACE is significantly changed from the native sequence. The polypeptide used for the co-crystallization consists only of residues 215-477, has two amino acid changes, and adds a Histidine tag to the C-terminus of the truncated polypeptide. Once the co-crystals with the specific associating compound were obtained, X-ray diffraction coordinates were obtained and reported for only amino acids 219-474 of the truncated polypeptide. The specification does not address the potential steric hinderance, or structure changing effects the missing 214 residues of the TACE polypeptide may have on the resulting crystal structure, nor does it discuss the effects of adding the Histidine tag. Histidines are highly charged, and would be expected to have significant interactions with its polypeptide environment. Finally, the mutations of a serine and glutamine to less charged residues alanine and glutamic acid would also be expected to have effects on any resulting structure due to the loss of charge.

As addressed previously, crystallization of proteins is a difficult, and non-exact science. Even having the crystal structure of one protein does not necessarily properly predict the nature

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and structure of a similar or mutated protein. (Gilliland et al. 1996 Current Opinion in Structural Biology Vol. 6 p 595-603) The effects of various changes to the protein are not always predictable, even by sophisticated computer modeling methods that were available at the time of the invention.

Applicant's work published after the filing of the instant application (Maskos et al. 1998 PNAS USA Vol 95 Pages 3408-3412: PTO-1449) draws no conclusions about the native TACE polypeptide, always referring to the catalytic domain, or their truncated co-crystals. Further, The reference indicates that the crystal structure of the truncated polypeptide "shows that TACE is not a typical member of the mammalian ADAMs but stands outside." (P 3412) This would indicate that conclusions or ideas generated for the ADAMs family of polypeptides may not be applicable to TACE catalytic domain polypeptides or native TACE polypeptides. This is a critical piece of information for the design of associating molecules. Maskos et al further separate the TACE polypeptide structure from known families of polypeptides in the discussion of the MMPs. Maskos et al. indicate that the structural homology between the catalytic domains of TACE and the MMP's is significantly lower than previously thought. This indicates that previous homology and structural design experiments were incorrect in their prediction that TACE had high structural homology to this family of known proteins. Finally, Maskos et al. state that "TACE exhibits, however, several structural peculiarities regarding surface charge and shape, which may enable the design of potent selective synthetic inhibitors." (emphasis added) This conclusion underscores the unpredictability of the prediction of protein structure, and the results of modeling inhibitors based on that prediction.

While working examples are not, per se, required, the specification must provide an enabling disclosure for the invention as it is now claimed. While the skill in the art of protein crystallography and computer structure analysis is high, that same art is highly unpredictable, and conclusions reached about one structure cannot necessarily be applied to another, even if there appears to be structural homology from computer predictions. The X-ray structure of the specific protein in question is required in order to assess those predictions with any accuracy. The claims do not set forth that specific X-ray structure, and are therefore not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43, 64, 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of the phrase "or a substantial part thereof" in reference to atomic coordinates are unclear. How much of the information in Table 1 represents a "substantial part"? How would one of skill in the art be able to determine where the cutoff is when eliminating data from Table 1? How much of the data from Table 1 is required to practice the invention is claimed? As such this limitation renders these claims indefinite.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 63, 41, 42, 45, and 66 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 15 of U.S. Patent No. 5,830,742. Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting claims all set forth methods comprising using a determined three-dimensional structure of a TACE peptide or catalytic domain to design an associating compound, that is also inhibitory.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 63, 41, 42, 45 and 66 are rejected under 35 U.S.C. 102(e) as being anticipated by Black et al. (US 5,830,742).

The applied reference has a common assignee but different inventive entity with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Black et al. disclose TACE polypeptides, catalytic subunits of TACE polypeptides, and methods of using the three dimensional structure of those polypeptides for the design of inhibitors. Therefore, Black et al. meet the limitations of the above rejected claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can generally be reached between the hours of 7:00 am and 1:00 pm Monday through Friday.

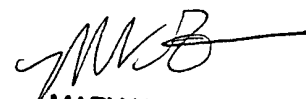
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028.

Official fax numbers for this Art Unit are: (703) 308-4242, (703) 872-9306. An *unofficial* fax number, direct to the Examiner is (703) 746 5279. Please call prior to use of this number.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the TC1600 Receptionist whose telephone number is (703) 308-0196.

mkz
1/9/02


MARY K. ZEMAN
PATENT EXAMINER
AU1631